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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,991	03/28/2001	Maurice Zauderer	1821.0050004	9763

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/818,991	ZAUDERER ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,22-30,43-62,64-68,73-109 and 138* is/are pending in the application.

4a) Of the above claim(s) *89-109* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,22-30,43-62,64-~~88~~ 68, 73-88 and 138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment and the response file don 4/2/04 has been fully considered and entered into the application.

2. Claims 11-21, 31-42, 63, 110-137 have been canceled and claims 1-10, 22-30, 43-62, 64-68, 73-109, 138 are currently pending in this application.

3. Claims 89-109 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/11/03.

4. Claims 1-10, 22-30, 43-62, 64-88 and 138 are currently being examined in this application.

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The specification indicates priority to several provisional applications. However, the oath/declaration does not acknowledge the priority to the provisional applications. A new oath/declaration is required in the body of which the present application and priority applications, should be identified by application number and filing date.

Specification

6. The disclosure is objected to because of the following informalities: in the specification page 43, paragraph 261 and page 45, paragraph 289, 291, SEQ ID Nos are missing.

Appropriate correction is required.

Withdrawn Claim Rejections

7. The written description rejection of claims 1-10, 22-30, 43, 59-62, 64-88 set forth in the previous office action mailed on 12/2/03, has been has been withdrawn.

NOTE that the rejection has been rewritten to address the newly amended claims.

8. The rejection of claims 69-70 under 35 U.S.C. 112, second paragraph has been withdrawn in view of amendments to the claims.

Maintained Claim Rejections

9. The art rejection of claims 1-10, 22-30, 43, 60, 62, 64-71, 76-79 under 35 U.S.C. 102(b) as being anticipated by US Patent 5,712,115 (HAWKINS et al), set forth in the previous office mailed on 12/2/03 has been maintained for the reasons of record.

10. The art rejection of claims 1-10, 22-30, 43-62, 64-88, and 138 under 35 U.S.C. 102(b) as being anticipated by US Patent 5,712,115 (HAWKINS et al), set forth in the previous office mailed on 12/2/03 has been maintained for the reasons of record.

New Claim Rejections Necessitated by the Amendment

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-10, 22-30, 43-62, 64-68, 73-88 and 138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The newly amended claim 1 recites '.....wherein said cell death is not the result of a cytotoxic T lymphocyte induced lytic event....'

The new limitation 'wherein said cell death is not the result of a cytotoxic T lymphocyte induced lytic event' claimed in Claim 1 has no clear support in the specification and the claims as originally filed. Applicants indicated that page 73 has support for the limitation, however the specification in page 73 discloses general selection methods, which has no clear support for the instantly claimed method. The subject matter claimed in claims alters the scope of the invention as originally disclosed in the specification.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

13. Claims 1-10, 22-30, 43, 59-62, 64-68, 73-88 and 138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim briefly recites a method of selecting a target polynucleotide comprising, a) introducing into a population of mammalian host cells a library of insert polynucleotides; the library is constructed in a poxvirus vector or a adenovirus vector or a herpesvirus vector; and the expression of target polynucleotide in the host cell promotes cell death; b) culturing the host cells and c) collecting the insert polynucleotides from host cells, and the cell death is not the result of a cytotoxic T lymphocyte induced lytic event.

The instant specification discloses the use of linear DNA virus vector such as vaccinia virus vector, and the cell death is the result of expression of a suicide gene product by the host cell. The specification discloses the 'tri-molecular recombination' method in the method of identifying the target polynucleotide. And further the specification discloses the use of host cells, which contain a death domain receptor expressed on the surface of host cells. The specification discloses that the suicide gene product is diphtheria toxin A subunit. The specification has not disclosed the use of any type of host cells in the method of screening for a target polypeptide whose expression promotes cell death, and the cell death is not the result of a cytotoxic T lymphocyte induced lytic event. The specification description is directed to the use specific host cells (which contain a cell death domain receptor) or RAW cells, and the use of Vaccinia virus vectors (especially vaccinia WR vectors) which clearly do not provide an adequate representation regarding the open ended claimed method for selecting a target polynucleotide of the instant claims. The specification description is directed to hypothetical methods of selecting target polynucleotides using generally known selection methods. The specification has no working examples of the instantly claimed method using the library of either pox virus vectors, adenovirus vector or a herpes virus vector, which is inserted into mammalian

cells and collecting inserted polynucleotides from the dead host cells, and the cell death is not the result of a cytotoxic T lymphocyte induced lytic event.

> With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to the instant method of screening; which requires a representative sample of showing of sufficient identifying characteristics of the products used to demonstrate possession of the claimed generic(s) and to demonstrate possession of products identified using the claimed method. In the present instance, the claimed invention contains no identifying characteristics regarding the identified polynucleotide or the host cells or the library of insert polynucleotides used. Additionally, the narrow scope of examples directed to the use of specific host cells (host cells contain cell death domain receptor) and specific vaccinia virus vectors, which are clearly not representative of the scope of the presently claimed method.

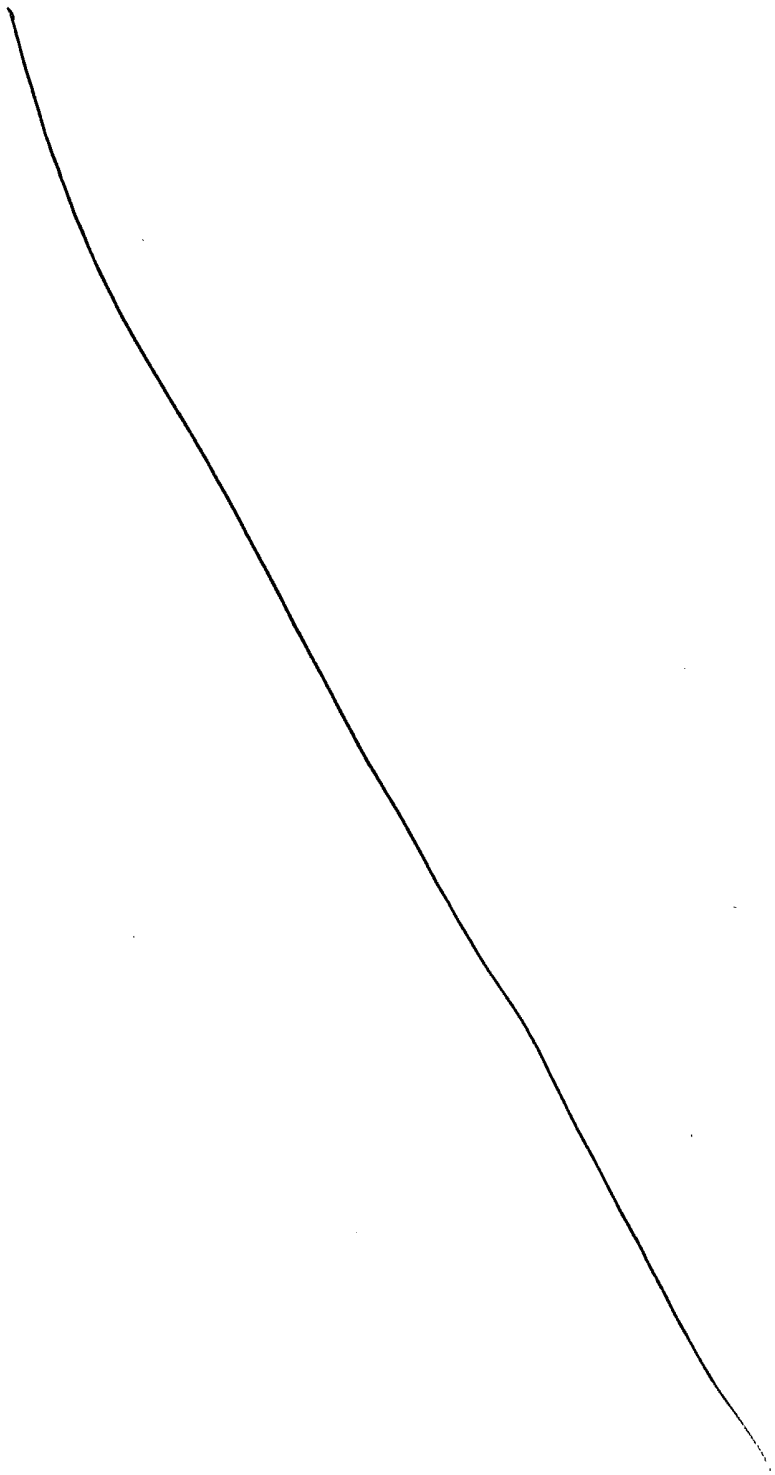
Response to Arguments

14. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

15. Applicant's arguments with respect to the written description rejection, have been considered but are moot in view of the new rejection necessitated by the amendment.

16. Applicant's arguments filed on 4/2/04, regarding the 35 USC. 102 (b) rejection over US Patent 5,712,115 (Hawkins et al) have been fully considered but they are not persuasive.

Claims 1-10, 22-30, 43, 60, 62, 64-71, 76-79 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,712,115 (HAWKINS et al).



The instant claim briefly recites a method of selecting a target polynucleotide comprising, a) introducing into a population of host cells a library of insert polynucleotides, and the expression of target polynucleotide in the host cell promotes cell death, b) culturing the host cells and c) collecting the insert polynucleotides from host cells.

Hawkins et al disclose human cell death associated protein (CDAP), which was isolated from rheumatoid synovium library. The reference discloses genetically engineered expression vectors (refers to the library of insert polynucleotides of the instant claims) and host cells comprising CDAP. The reference discloses that nucleotide sequence encoding CDAP is inserted into an appropriate expression vector, which contain necessary elements for transcription and translation of inserted coding sequence. The reference discloses that in mammalian host cells, a number of viral based expression systems may be utilized, the reference especially teaches the use of adenovirus vectors (i.e., see column 11). The reference discloses that host cells transformed with a CDAP nucleotide sequence may be cultured under conditions suitable for the expression and recovery of the encoded protein from the cell culture (refers to instant claims 27-30). The protein produced by a recombinant cell may be secreted or contained intracellularly depending on the sequence and/or vector used (i.e., see column 13). The reference discloses that the host cells which contain the coding sequence for CDAP and express CDAP may be identified by a variety of procedures known to those of skill in the art (i.e., see column 12). The reference discloses that the CDAP can be assayed in BHK cells seeded on a microscopic cover slip (refers to the instant claims 7-9, 26) and transiently transfected with plasmid engineered to give rich expression, and the nuclei which express CDAP noticed to be apoptotic (i.e., see column 12) (refers to the instant claim method step c), and in column 13 the reference discloses the methods for purification of CDAP from host cells. Thus, the reference clearly anticipates the claimed invention.

Applicants argue that the reference does not teach or suggest a selection method, comprising introducing a polynucleotide library into mammalian cells, culturing the cells, and collecting the inserted polynucleotides from the host cells that undergo the cell death.

Applicant's arguments have been considered and are not persuasive, since the reference clearly teach that the selection method. The reference discloses in column 9, ('Expression Systems') that 'In order to express a biologically active CDAP, the nucleotide sequence

encoding CDAP, or a functional equivalent, is inserted into an appropriate expression vector. A variety of expression vector/host systems may be utilized to contain and express a CDAP coding sequence. The reference, i.e., in column 11 teaches the mammalian host cells, and viral expression systems used in the invention. The reference further teaches that 'any number of selection systems may be used to recover transformed cell lines. The reference teaches in the section 'Identification of Transformants containing the polynucleotide sequence' (column 12), teaches '...alternatively, host cells which contain the coding sequence for CDAP and express CDAP may be identified (refers to the selection method of the instant claims) by a variety of procedures. The reference teaches that using a microscope and stain, those nucleic which express CDAP appear apoptotic (refers to 'host cells which undergo cell death'). The reference further teaches that 'host cells transformed with a CDAP nucleotide sequence may be cultured under conditions suitable for the expression (refers to the instant claim step b) and recovery (refers to the step c of the instant claims) of the encoded protein from cell culture (i.e., see column 13). Thus the reference clearly teaches all the limitations of the instant claims, and the rejection of the record has been maintained.

17. Applicant's arguments filed on 4/2/04, regarding the rejection of claims over Zauderer (US Pub No: 2003/0133917 A1) have been fully considered but they are not persuasive.

Claims 1-10, 22-30, 43-62, 64-88 and 138 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2003/0133917 A1 (ZAUDERER).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in

the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claim briefly recites a method of selecting a target polynucleotide comprising, a) introducing into a population of host cells a library of insert polynucleotides, and the expression of target polynucleotide in the host cell promotes cell death, b) culturing the host cells and c) collecting the insert polynucleotides from host cells.

Zauderer discloses novel methods for the identification of antigens recognized by CTLs and specific for human tumors, cancers and infected cells. The reference discloses engineering of recombinant viruses as expression vectors for tumor, cancer or infected cell-specific antigens. The reference discloses that the tumor specific CTLs generated as described can be used to screen expression libraries prepared from target tumor cells (refers to the instant library of target insert polynucleotides) to identify clones encoding the target epitope(i.e., see paragraph 54 and 56 in page 6). The reference discloses the DNA library is constructed in vaccinia virus vectors, preferably trimolecular recombination method employing modified vaccinia virus vectors (i.e., see paragraph 57 in page 7). The reference discloses that the method is used to select for those cells infected with the recombinant virus that express the target epitopes of the specific cytotoxic T cells. An adherent monolayer of cells (refers to the host cells on solid support of the instant claims) is infected with recombinant viral vector library, e.g., vaccinia recombinant viral library as m.o.i. less than or equal to 1 (refers to instant claim 61) (i.e., see page 7, paragraph 59). The reference discloses that the some of the cells infected with recombinant particle leads to expression of the target epitope and undergo a lytic event. The cells which undergo the lytic event or released from the monolayer and can be harvested in the floating cell population. The above described protocol is repeated for preferably five or more cycles to increase the level of enrichment obtained by this process (refers to the instant claim 3) (i.e., see page 7, paragraph 60). The reference clearly anticipates the claimed invention.

Applicants argue that claim 1 has been amended to recite " wherein said cell death is not the result of a cytotoxic T lymphocyte-induced lytic event", therefore, the rejection is moot.

Applicants arguments are not persuasive, since the support for the newly claimed limitation has not been found in the originally filed specification or the claims. The rejection will

be withdrawn in the event applicants show the support for the newly added limitations in the specification and the new matter rejection has been withdrawn.

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

PADMASHRI PONNALURI
PRIMARY EXAMINER

Pp
11 June 2004